

DOCUMENT-IDENTIFIER: US 20020144939 A1

TITLE: Miniaturized blood centrifuge having side  
mounted motor  
with belt drive

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Detail Description Paragraph - DETX (144):

[0274] Phase-one according to the preferred embodiment (FIG. 62) begins by restoring the clot-forming process. To accomplish this, an agent (restoration agent) capable of reversing the effects of the anticoagulation agent is added back into the first portion of the platelet rich plasma 260 stored in vessel 952. Preferably, the restoration agent can be vessel 952 itself or the restoration agent is contained within vessel 952 prior to the introduction of platelet rich plasma 260; however, the restoration agent may also be introduced later. It is furthermore preferable that the contact activator be a material such as but not limited to glass wool 953 or silica, aluminum, diatomaceous earth, kaolin, etc., or non-wettable surfaces such as plastic,

siliconized glass, etc. Chemical activators, such as kaolin, can also be used to speed up the clotting time; however, their subsequent removal would also be necessary. In the preferred embodiment, a plastic syringe is the preferred container used to collect the desired fraction. In the presently preferred embodiment of the invention, the reversal of the anticoagulant is accomplished using calcium chloride. However, any substance which is known or found to be functionally equivalent to calcium chloride, such as, calcium gluconate or calcium carbonate, in restoring the coagulation activity of citrated blood may be used in the practice of the present invention. Thus, although calcium chloride is the presently preferred calcium salt for use in the invention, any calcium salt which functions in a similar manner to calcium chloride may be used in the invention. Similarly, although many blood coagulation reactions are currently believed to require calcium ions as cofactors, any substance which is known or subsequently found to be functionally equivalent to calcium in facilitating these coagulation reactions may be used, either individually or in combination with calcium, in the practice of the present invention. If the

anticoagulation  
agent used was heparin, then heparinase or any other suitable  
anticoagulant  
reversing compound would be used to reverse the effect of the  
anticoagulation  
agent. The concentration of the restoration agent used to reverse  
the  
anticoagulation will depend in part, upon the concentration of the  
anticoagulation agent in the platelet rich plasma 260 and the  
stoichiometry of  
the chelating and coagulation reactions. However, the  
concentration of the  
restoration agent used to reverse the anticoagulation must be  
sufficient to  
achieve clot formation.

the bioadhesive sealant will be applied. First, a platelet rich plasma and a platelet poor plasma are formed by centrifuging a quantity of anticoagulated whole blood that was previously drawn from the patient. The platelet rich plasma and platelet poor plasma are then divided into two portions. To the first portion, which is used in phase-one, a compound that reverses the effect of the anticoagulant is added, and a clot is allowed to form. The clot is then triturated and the resulting serum, containing autologous thrombin, is collected. The serum obtained from phase-one is then mixed with the second portion of the platelet rich plasma or platelet poor plasma, used in phase-two, to form the bioadhesive sealant of the present invention.

66 Claims, 10 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 7

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TITLE: Autologous fibrin sealant and method for making the same

DATE-ISSUED: September 3, 2002

INVENTOR-INFORMATION:

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APPL-NO: 09/ 063338

DATE FILED: April 20, 1998

PARENT-CASE:

CROSS-REFERENCE TO OTHER APPLICATIONS

This patent application is a continuation-in-part of U.S. patent application Ser. No. 08/640,278, filed Apr. 30, 1996, now abandoned, and entitled Method For Making Autologous Fibrin Sealant.

INT-CL: [07] A61K035/16

US-CL-ISSUED: 424/530, 424/529 , 424/531 , 424/532

US-CL-CURRENT: 424/530, 424/529 , 424/531 , 424/532

FIELD-OF-SEARCH: 424/529; 424/530 ; 424/531 ; 424/532

REF-CITED:

U.S. PATENT DOCUMENTS

| PAT-NO  | ISSUE-DATE    | PATENTEE-NAME  |
|---------|---------------|----------------|
| US-CL   |               |                |
| 4627879 | December 1986 | Rose           |
| N/A     | N/A           | N/A            |
| 5354682 | October 1994  | Kingdon et al. |
| N/A     | N/A           | N/A            |
| 5391380 | February 1995 | Barrow et al.  |
| 424/570 | N/A           | N/A            |
| 5510102 | April 1996    | Cochrum        |

|           |               |                   |       |
|-----------|---------------|-------------------|-------|
| 424/78.08 | N/A           | N/A               |       |
| 5585007   | December 1996 | Antanavich et al. |       |
| 210/782   | N/A           | N/A               |       |
| 5607694   | March 1997    | Marx              | N/A   |
| N/A       | N/A           |                   |       |
| 5643192   | July 1997     | Hirsh et al.      | 604/4 |
| N/A       | N/A           |                   |       |
| 5788662   | August 1998   | Antanavich et al. | 604/6 |
| N/A       | N/A           |                   |       |

#### FOREIGN PATENT DOCUMENTS

| FOREIGN-PAT-NO | PUBN-DATE   | COUNTRY |
|----------------|-------------|---------|
| US-CL          |             |         |
| 0 443 724      | August 1991 | EP      |
| 2 696 095      | April 1994  | FR      |
| WO 97/29792    | August 1997 | WO      |

#### OTHER PUBLICATIONS

Marieb, E., Human Anatomy and Physiology, 2d Ed.,  
Benjamin/Cummings,  
California, 1992, pp. 596-596.\*

"Simultaneous Occurrence of Human Antibodies Directed  
against Fibrinogen,  
Thrombin, and Factor V Following Exposure to Bovine Thrombin:  
Effects on Blood  
Coagulation, Protein C Activation and Platelet Function," Vibhuti  
D. Chouhan,  
Raul A. De La Cadena, Chandrasekaran Nagaswami, John W.  
Weisel, Mehdi Kajani,

and A. Koneti Rao, Thrombosis and Haemostasis, 77(2):343-9 (1997).

"Severe Bleeding due to Factor V Inhibitor after Repeated Operations Using Fibrin Sealant containing Bovine Thrombin," W. Muntean, W. Zenz, G. Edlinger, and A Beitzke, Thrombosis and Haemostasis, 77:1223 (1997).

Postoperative Bleeding Induced by Topical Bovine Thrombin: Report of Two Cases, Robert J. Christie, MD, Leonthena Carrington, BS, and Barbara Alving, MD, Surgergy, 121(6):708-710 (Jun. 1977).

"Fibrin Sealant: Summary of a Conference on Characteristics and Clinical Uses," B.M. Alving, M.J. Weinstein, J.S. Finlayson, J.E. Menitove, and J.C. Fratantoni, Transfusion, 35:783-790 (1995).

"Inhibitor to Factor V after Exposure to Fibrin Sealant During Cardiac Surgery in a Two-Year-Old Child," W. Muntean, W. Zenz, K. Finging, G. Zobel, and A Beitzke, Acta Paediatr, 83:84-7 (1994).

"Immunization by Bovine Thrombin Used With Fibrin Glue During Cardiovascular Operations," Micheline Berruyer, BS, Jean Amiral, PhD, Patrick Ffrench, MD, Jean Belleville, MD, Olivier Bastien, MD, Jean



Clerc,MD, Alain

Kassir, MD, Susanne Estanove, MD, and Marc Dechavanne, MD,  
The Journey of

Thoracic and Cardiovascular Surgery, 105(5):892-897 (May  
1993).

"An Anaphylactic Reaction to Topical Fibrin Glue," Hiromasa  
Mitsuhata, MD,

Yuji Horiguchi, MD, Kazuhiko Saitoh, MD, Hirokazu Fukuda,  
MD, Yoshihiro

Hirabayasi, MD, Hideaki Togashi, MD, and Reiju Shimizu, MD,  
Anesthesiology,

81(4):1074-1077 (Oct. 1994).

"Anaphylactic Reaction to Topical Bovine Thrombin," David  
M. Rothenberg,

MD, and James N. Moy, MD, Anesthesiology, 78(4):779-782  
(Apr. 1993).

"Clinical Significance of Antibodies to Bovine and Human  
Thrombin and

Factor V After Surgical Use of Bovine Thrombin," Samuel I.  
Rapaport, MD,

Ariella Zivelin, M.Sc., Robert A. Minow, MD, Christine S.  
Hunter, MD, and

Kathleen Donnelly, MS, A.J.C.P., 97(1):84-91 (Jan. 1992).

"Development of Antibodies to Thrombin and Factor V With  
Recurrent Bleeding

in a Patient Exposed to Topical Bovine Thrombin," James L.  
Zehnder, and

Lawrence L.K. Leung, Blood, 76(10):2011-2016 (Nov.15, 1990).

"An Anaphylactic Reaction to Fibrin Glue," Leslie Newberg Milde, MD, Anesth Analg, 69:684-6 (1989).

"Iatrogenic Immunization with Bovine Thrombin: A Mechanism for Prolonged Thrombin Times after Surgery," Michael J. Flaherty, MD, Ruth Henderson, and Mark H. Wener, MD, Annals of Internal Medicine, 111(8):631-634 (Oct.15, 1989).

"Clinical Application of The Fibrin Adhesive," Suzuki, M., et al., Otolaryngology, 56(11)949-953 (1984), Tokyo.

ART-UNIT: 1651

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ABSTRACT:

In general, the present invention relates to a two-phase method for forming an autologous bioadhesive sealant composition or fibrin glue wherein all of the blood components for the bioadhesive sealant are derived from a patient to whom